studied, all of them showed clinical alterations, cytological changes, both or partners with lesions. The samples were taken by sterilized swabs (Viratype. Digene). For PCR, oligonucleotides primers MY09 and MY011 were used, which recognize L1 viral region. The viral typification was achieved by using Sharp Signal detection system (Digene), which recognizes virus of low oncogenical risk: 6, 11, 42, 43, 44; intermediate/high oncogenical risk: 16, 18, 31, 33, 35, 45, 51, 52, 53, 56, and 58.

Results: In the 66.6% (80/120) of patients was observed the presence of the viral genome and 33.3% (40/120) of the patients were negative for HPV ($p < 0.0001$). In the subgroup of patients with no morfological changes, it was found viral DNA in 40% of the samples, from which 23.3% showed HPV high risk type (HR), 3.3% of low risk (LR) and 13.3% were not typified. In patients with Low Grade Intraepithelial Lesions (LSIL) was found HPV in 70% of the samples (HR = 56.6%, LR = 3.75% and Not typified = 15%). In the subgroup with High Grade Intraepithelial Lesions (HSIL) was observed the presence of HPV in the 80% of all samples (HR = 50% and Not Typified = 30%).

P1138 Detection of Human Papillomavirus (HPV) in Genital Lesions

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Introduction: Specific HPV types are associated with the development of genital lesions. Amongst these, some HPV types (16, 18, 31, 33 and 54) are strongly associated with cervical carcinoma (zur Hausen 1989).

Objective: To study the incidence of HPV High-Intermediate Risk (H.R) and Low Risk (L.R) in genital lesions, by hybrid capture system.

Patients and Methods: Fifty clinical specimens of cervix (biopsies or scrapes) of women with an average (33 ± 9.9) years old, were grouped as follows: group 1 (n = 12), Koilocytosis; group 2 (n = 12), Cervical Intraepithelial Neoplasia (CIN I); group 3 (n = 13) CIN II–III; group 4 (n = 13), Epidermoid Carcinoma.

HPV DNA detection was made through a chemiluminescent molecular hybridization method with concensus probes for Low Risk (6/11/42/43/44) and High-Intermediate Risk (16/18/31/33/35/45/51/52/56). Group 4 was hybridized with individual probes (HPV 16 and HPV 18) with crossreactivity control.

Results: The results in different patient groups were:

(1) group 1 – 6/12 (50%) were positive for HPV (H.R) type and 4/12 (33.3%) were positive for HPV (L.R) type
(2) group 2 – 8/12 (67%) were positive for HPV (H.R) type and 2/12 (16.6%) were positive for HPV (L.R) type
(3) group 3 – 9/43 (70%) were positive for HPV (H.R) type and 2/13 (15.3%) were positive for HPV (L.R) type
(4) group 4 – 13/13 (100%) were positive for HPV (H.R) type

In the group 4, the use of individual probes showed that:

6/13 (46%) were HPV 16 positive and 3/13 (23%) were HPV 18 positive

Conclusion: These results suggest that there is a correlation between High-Risk HPV infection and aggressive types of lesion.

New quinolones II

P1139 Comparative *In Vitro* Activity of Trovafloxacin Against Fresh Bacterial Isolates from Pediatric Patients

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Trovafloxacin (TRO) is a novel fluoronapthyridone antibiotic. In comparison with fluoroquinolones, TRO has an enhanced activity against Gram-positive and anaerobic pathogens. It displays favourable pharmacokinetic properties, enabling once-daily administration.

In this study, the *in vitro* activities of TRO in comparison with ciprofloxacin (CIP), imipenem (IMI), and ceftazidime (CTAZ) were determined against 495 fresh bacterial isolates from pediatric patients. Standard microdilution techniques with Mueller-Hinton broth or Standard-1 broth #7882, Merck (indicated with *) were used. MIC_{50} and MIC_{90} values for the most commonly isolated pathogens were:

	n	TRO 50%/90%	CIP 50%/90%	IMI 50%/90%	CTAZ 50%/90%
S. pneumoniae	26	0.12/0.12	0.03/1	1/2	0.25/0.5
E. faecalis	32	0.12/1	0.5/1	1/2	32/32
E. faecium	28	1/8	32/32	4/32	32/32
S. aureus	52	0.03/0.03	0.25/0.25	0.03/0.12	8/8
S. epidermidis	52	0.03/2	0.12/16	0.25/32	32/32
P. aeruginosa	50	0.25/0.5	0.25/1	0.5/2	2/4
E. coli	56	0.03/0.03	0.003/0.03	0.12/0.25	0.25/4
Enterobacter spp.	34	0.03/0.12	0.12/0.25	0.06/0.25	0.5/32
K. pneumoniae	30	0.03/0.5	0.12/0.25	0.03/0.25	0.12/32
P. mirabilis	30	0.25/0.25	2/2	0.03/4	0.03/0.06
*H. influenzae**	31	0.03/0.03	0.03/0.5	0.25/1	0.12/0.12

TRO was the most active antibiotic against Gram-positive pathogens. Against Gram-negative pathogens, TRO was as active as CIP and IMI, and more active than CTAZ.

P1140 Trovafloxacin: In Vitro Anti-Anaerobic Activity Including Spectrum, Bactericidal Activity, and Mutational Frequency

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Currently marketed fluoroquinolones including ciprofloxacin and ofloxacin have wide-spectrum activity against aerobic gram-negative bacilli but poor activity against clinically important anaerobes. Trovafloxacin is a new azabicyclo-naphthyridone with an expanded spectrum against aerobes.

Objectives: To compare the activity of trovafloxacin and other antimicrobials against various clinically important anaerobes.

Methods: A total of 590 clinical isolates of anaerobes from various sources were tested using an NCCLS recommended broth microdilution procedure.

Results: Trovafloxacin was highly active against all species with a mode MIC of 0.25 μg/ml, an MIC_{90} of 1 μg/ml, and inhibited 97% of the *B. fragilis* group at 2 μg/ml. Trovafloxacin had comparable activity to metronidazole and was 8- to 64-fold more active than ampicillin/sulbactam, clindamycin, ciprofloxacin, cefoxitin, and cefotetan overall including strains of *Clostridium, Fusobacterium, Porphyromonas,* and *Prevotella*. Bactericidal activity of trovafloxacin was concentration-dependent and showed progressive bactericidal activity against the *B. fragilis* group at 4x and 8x MIC over 24 hr. The mutational frequency of *B. fragilis* strains to trovafloxacin was $<10^7$ at 8× and 12× MIC. Little effect on trovafloxacin was noted at different pH's, inoculum sizes, and increased protein concentrations.

Conclusions: These data indicate that trovafloxacin may be potentially useful in mixed aerobic/anaerobic infections.

P1141 Susceptibility of Selected Bacteria Against Trovafloxacin and Ciprofloxacin as Determined Using the E-test

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Using the E-test, we have compared minimum inhibitory concentrations (MIC's, mg/L) of trovafloxacin (TRO), Ciprofloxacin (CIP) and, in part, Ceftriaxone (CRO) against methicillin-resistant *Staphylococcus aureus* (MRSA; N = 190), *Streptococcus pneumoniae* (N = 332), *Enterobacteriaceae* infrequently encountered in clinical specimens (N = 213), and diarrheagenic organisms (N = 179) including enterotoxigenic (ETEC), verotoxigenic (VTEC) and enteroinvasive *E. coli* (EIEC), *Aeromonas, Campylobacter, Salmonella, Shigella* and *Yersinia* species.

Against MRSA, MIC50/MIC90 were 1.5/≥32 for CIP, 0.094/≥32 for TRO, and ≥256/≥256 for CRO. With *S. pneumoniae* the respective values were 0.75/1.5 for CIP, 0.125/0.19 for TRO, and 0.016/0.032 for CRO. The percentage of strains susceptible against TRO (utilized/proposed breakpoints were ≤2 mg/l for susceptibility and ≥8 mg/l for resistance), CIP and CRO was 100, 87.3 and 98.2 for *S. pneumoniae* and 77.4, 48.9 and 37.9 for MRSA, respectively.

All Gram-negative bacteria (including 10 erythromycin-resistant *Campylobacter jejuni/coli*) were fully susceptible against both TRO (range ≤0.002–1.5) and CIP (range ≤0.002–0.38) with MIC's being slightly lower for CIP than for TRO.

Conclusion: TRO is more active than CIP against the Gram-positive bacteria and comparable to or slightly less active than CIP against the Gram-negative organisms tested.

P1142 Comparative In Vitro Activities of Trovafloxacin and 16 Other Antibiotics Against Penicillin Intermediate (PISP) and Penicillin Resistant (PRSP) *Streptococcus pneumoniae* Isolates

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The activity of Trovafloxacin was compared to 16 other antibiotics against 43 consecutive isolates (18 PRSP and 25 PISP). Minimal inhibitory concentrations were evaluated by microbroth dilution using Mueller Hinton Broth supplemented by 3% Lysed Horse Blood.

	MIC_{90}			MIC_{90}	
	PISP	PRSP		PISP	PRSP
Trovafloxacin	0.25	0.25	Cefotaxime	0.5	1
Ciprofloxacin	4	2	Ceftriaxone	0.5	2
Clinafloxacin	0.06	<0.03	Ceftizoxime	8	16
Sparfloxacin	2	1	Ceftazidime	16	64
Penicillin	1	16	Cefixime	16	64
Imipenem	1	1	Cefpodoxime	2	8
Meropenem	2	8	Ramoplanin	0.25	0.25
Synercid	0.5	1	Teichoplanin	0.5	0.13
Vancomycin	1	0.5			

Many antibiotics demonstrate good in vitro activity yet substantial differences can be observed within the same class of antimicrobial agents. For the quinolones Clinafloxacin > Trovaflaxcin > Sparfloxacin > Ciprofloxacin. In view of achievable serum levels Trovafloxacin and Clinafloxacin should be considered for clinical trials of *Streptococcus pneumoniae* including PISP and PRSP.

P1143 Susceptibility of Selected Bacteria Against Trovafloxacin and Ciprofloxacin as Determined Using the E-test

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Using the E-test, we compared minimum inhibitory concentrations (MICs, mg/l) of trovafloxacin (TRO), ciprofloxacin (CIP) and, in part, ceftriaxone (CRO) against methicillin-resistant *Staphylococcus aureus* (MRSA; N = 190), *Streptococcus pneumoniae* (N = 332), Enterobacteriaceae infrequently encountered in clinical specimens (N = 213), and diarrheagenic organisms (N = 179) including enterotoxigenic (ETEC), verotoxigenic (VTEC) and enteroinvasive *E. coli* (EIEC), *Aeromonas, Campylobacter, Salmonella, Shigella* and *Yersinia* species.

Against MRSA, MIC_{50}/MIC_{90} were 0.094/>32 mg/l for TRO, 1.5/>32 mg/l for CIP, and >256/>256 mg/l for CRO. For *S. pneumoniae,* the respective values were 0.125/0.19 mg/l for TRO, 0.75/1.5 mg/l for CIP, and 0.016/0.032 mg/l for CRO. The percentages of strains susceptible against TRO (utilized/proposed breakpoints were <2 mg/l for susceptibility and >8 mg/l for resistance), CIP and CRO were 100%, 87.3 and 98.2% for *S. pneumoniae,* and 77.4%, 48.9% and 37.9% for MRSA, respectively.

All Gram-negative bacteria (including 10 erythromycin-resistant *Campylobacter jejuni/coli*) were fully susceptible to both TRO (<0.002–1.5 mg/l) and CIP (<0.002–0.38 mg/l) with MICs being slightly lower for CIP than for TRO.

Conclusion: TRO is more active that CIP against Gram-positive bacteria and comparable to, or slightly less active than, CIP against Gram-negative organisms tested.

P1144 Comparative In Vitro Activities of Trovafloxacin

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Objective: To study the in vitro antibacterial activities of trovafloxacin, a new fluoronaphilidine quinolone and compare them with other quinolones and relevant comparative agents.

Methods: A total of 655 recent clinical isolates were tested for minimum inhibitory concentrations (MICs) by standard agar dilution technique (NCCLS) or E-test (AB Biodisk) with 17 antimicrobial agents.

Results: For gram-positive cocci; *S. aureus* (MSSA), enterococci, PSSP and PRSP, the MIC_{50} of trovafloxacin, ofloxacin and ciprofloxacin were 0.025–0.25, 0.5–4 and 0.5–2 μg/ml, respectively. Trovafloxacin's MICs were 6–20 times lower than ofloxacin and ciprofloxacin. The MICs of trovafloxacin against gram-negative cocci, *N. gonorrhoeae* (PPNG and NPPNG) were similar to those of ofloxacin and ciprofloxacin (0.0025–0.01 μg/ml). For glucose-fermenting gram-negative bacilli, including *E. coli, K. pneumoniae* and *Enterobacter* spp., the MIC_{50} of trovafloxacin, ofloxacin, ciprofloxacin and amikacin were 0.01–0.025, 0.05–0.25, 0.025–0.05 and 2–4 μg/ml, respectively. Trovafloxacin's MICs were almost equal to ciprofloxacin's against most species of the *Enterobacteriaceae,* except against *Morganella, Proteus* and *Providencia,* trovafloxacin's MICs were higher than ciprofloxcain's. For non-fermenters, the MIC_{50} of trovafloxacin, ofloxacin, ciprofloxacin, amikacin and ceftazidime were 0.05–2, 0.25–8, 0.5–8, 4–64 and 2–32 μg/ml. Within the group of non-fermenters, *A. baumannii* was the most susceptible (MIC_{50} = 0.05 μg/ml) and B. pseudomallei was the most resistant (MIC_{50} = 2 μg/ml).

Conclusions: Trovafloxacin showed good activities against both gram-positive and gram-negative bacteria. Trovafloxacin extened its spectrum to cover *S. aureus* (MSSA), *S. pneumoniae* (PSSP and PRSP)

and enterococci except for MRSA when standard agents was clearly superior. Trovafloxacin exert good intrinsic potency (MIC_{50}) against glucose-fermenting gram-negative bacilli, *P. aeruginosa, A. baumannii* and *S. maltophilia.*

P1145 In Vitro Activity of Trovafloxacin and Five Other Fluoroquinolones

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Objectives: to assess the in vitro inhibitory and bactericidal activities of trovafloxacin and five other fluoroquinolones (ciprofloxacin, ofloxacin, pefloxacin, rufloxacin, and sparfloxacin) against a wide range of clinical isolates from Italian hospitals.

Methods: MICs (microdilution method) and MBCs were determined by standard procedures as recommended by NCCLS.

Results: Against gram-positive bacteria, trovafloxacin was overall more active than the other antibiotics tested, including sparfloxacin, another gram-positive-oriented fluoroquinolone, and was active against all ciprofloxacin-resistant streptococci, enterococci and listeriae, all ciprofloxacin-resistant *Staphylococcus aureus* isolates, and most ciprofloxacin-resistant coagulase-negative staphylococci. Its antistaphylococcal activity was not affected by oxacillin resistance or susceptibility of the isolates, nor its antipneumococcal activity by whether isolates were susceptible or resistant to penicillin. Against gram-negative bacteria, trovafloxacin retained a high potency, mostly comparable with that of ciprofloxacin. Rufloxacin and pefloxacin were less active than the other fluoroquinolones against most test strains of both gram-positive and gram-negative organisms. Trovafloxacin MBCs usually equalled or exceeded by 2 to 4 times the MIC values, indicating that the compound is overall highly bactericidal.

Conclusion: In vivo studies and clinical trials with trovafloxacin are warranted and strongly urged.

P1146 *In vitro* Activity of Levofloxacin Against Isolates from Patients with Community Acquired Lower Respiratory Tract Infections

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We cultured cito-bacteriologically valid sputums, BAL, brush protected aspirates, pleural fluid and/or blood from 69 patients with community acquired pneumonia (CAP} and valid sputum from 154 patients with acute exacerbations of chronic bronchitis (AECB). Eubacteria were recovered significatively from 31 CAP (45%) and 94 AECB (61%). The four predominant species among CAP were *S. pneumoniae* (Sp) 67%; *H. influenzae* (Hi) 13%;*Klebsiella spp.* (Kp) and *S. aureus* (Sa) 6.5% each and among AECB: Sp 37%; *M. catarrhalis* (Mc) 29; Hi 18 and *P. aeruginosa* (Pa) 10. MICs were determined by microdilution or Etest for oral antimicrobials against the 125 CAP and AECB isolates. Overall susceptibility (S) percentages were for; levofloxacin (LV) 97; ciprofloxacin (CP) 95; ofloxacin (OF) 95; azithromycin (AZ) 88; roxithromycin (RO) and clarithromycin (CL) 87; cefuroxime (FU) 86; amoxicillin-clavulanate (AC) 80 and cefixime (FI) 75. We also compared the activity of LV against 60 Sp (40 penicillin unsusceptible) LV showed 100% S; OF 92; CP 82; CL and RO 96; AZ 94; AC 96; FU 80 and FI 35. We also demostrated that LV showed 100% S against 20Mc, 20Hi, 20SAMS and was the activiest drug against 20 Kp (95% S) and 20 Pa (92% S).

P1147 *In Vitro* Bacteriostatic Activity of Levofloxacin and Three Other Fluoroquinolones against Penicillin-Susceptible and Penicillin-Resistant *Streptococcus pneumoniae*

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Worldwide spread of pneumococcal penicillin resistance has led to a need for therapeutic alternatives and new quinolones may be useful for infections caused by resistant pneumococci. The purpose of this study was to investigate the susceptibility to levofloxacin (LVFX), ofloxacin (OFX), sparfloxacin (SPFX) and ciprofloxacin (CIP) of 205 strains (101 penicillin-susceptible [PS], 51 penicillin-intermediate-resistant [PIR], 53 penicillin-resistant [PR]) that had been sent by French hospitals participating in the National Cooperative Survey of Pneumococcal Infections between September 1996 and October 1996. The determination of MICs (mg/l) was made by the agar dilution method. The comparative activities of the 4 drugs were as follows:

	PS			PIR			PR		
	MIC_{50}	MIC_{90}	Range	MIC_{50}	MIC_{90}	Range	MIC_{50}	MIC_{90}	Range
SPFX	0.25	0.5	0.06–0.5	0.25	0.25	0.06–0.5	0.25	0.25	0.12–8
CIP	0.5	1	0.25–2	0.5	1	0.12–1	0.5	1	0.25–16
LVFX	1	1	0.25–1	0.5	1	0.25–1	1	1	0.5–16
OFX	1	2	0.5–2	1	2	0.5–2	1	2	1–32

A total of 204 of the strains had a LVFX MIC between 0.25 mg/l and 1 mg/l and only one of the 205 strains was highly resistant (MIC = 16 mg/l). Whatever the level of susceptibility to penicillin (PS/PIR/PR) the relative bacteriostatic activity for the four drugs was: SPFX > CIP > LVFX > OFX.

P1148 Comparative *In vitro* Activity of Levofloxacin (LV) Against Isolates from Adult Patients with Community-acquired Lower Respiratory Tract Infections (CLRTI)

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We cultured bacteriologically-validated sputums, BAL, brush-protected aspirates, pleural fluid and/or blood from 69 patients with community-acquired pneumonia (CAP) and bacteriologically-validated sputum from 154 patients with acute exacerbations of chronic bronchitis (AECB).

Significant numbers of Eubacteria were recovered from 31 CAP (45%) and 94 AECB (61%) specimens. The 4 predominant species in the CAP specimens were *S. pneumoniae spp.* (Sp, 67%), *H. influenzae* (Hi, 13%), *K. pneumoniae* (Kp, 6.5%) and *S. aureus* (Sa, 6.5%). AECB isolates consisted of Sp (37%), *M. catarrhalis* (Mc, 29%), Hi (18%) and *P. aeruginosa* (Pa, 10%). MICs were determined by microdilution or E-test for oral antimicrobials against the 125 CLRTI isolates. The overall susceptibility percentages of the CLRTI isolates were: LV 97%, ciprofloxacin (CP) 95%, ofloxacin (OF) 95%, azithromycin (AZ) 88%, roxithromycin (RO) 87%, clarithromycin (CL) 87%, cefuroxime (FU) 86%, amoxicillin-clavulanate (AC) 80%

and cefixime (FI) 75%. We also compared the activity of LV and other agents against 60 Sp (of which 40 were unsusceptible to penicillin). These isolates showed 100% susceptibility to LV, 92% to OF, 82% to CP, 96% to CL and RO, 94% to AZ, 96% to AC, 80% to FU and 85% to FI. We also demonstrated that 20 Mc, 20 Hi and 20 methicillin-susceptible Sa isolates were 100% susceptible to LV. Furthermore, LV was the most effective drug against 20 Kp (95% susceptibility) and 20 Pa (92%) isolates.

P1149 The Bactericidal Activity of Levofloxacin and Other Fluoroquinolones against *Streptococcus pneumoniae*

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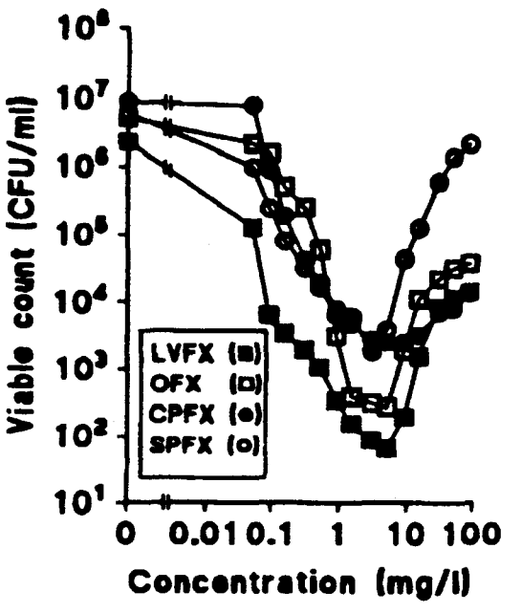
The emergence of penicillin-resistant (pen-res) *Streptococcus pneumoniae* (SP) has become a problem over recent years. To overcome this, new drugs such as the fluoroquinolones (FLQs) are being considered for the treatment of SP infections. In this study, the bactericidal activity of levofloxacin (LVFX), ofloxacin (OFX), ciprofloxacin (CPFX) and sparfloxacin (SPFX) was investigated against 4 strains of SP (pen MIC, mg/l): SP C3LN4 (0.0075), SP 269 (0.0075), SP 1600 (0.1), SP KPR (2). Bactericidal activity was determined against SP (at about 10^6 CFU/ml) in nutrient broth plus laked horse blood (7%) for 3 h at 37°C. The results for SP C3LN4 are shown in Fig. 1. LVFX was the most bactericidal drug tested against SP C3LN4, followed by OFX, CPFX and SPFX, in that order of potency. Similar results were obtained with the other strains, including the pen-res strain. This suggests that pen-res does not affect the potency of FLQs against SP. Therefore, FLQs would be a good option for pen-res SP therapy. Of the 4 drugs tested, LVFX would appear to be the FLQ of choice against such infections. These findings warrant further clinical evaluation of LVFX in the treatment of SP infections.



P1150 Results of a European Multicentre Study of the Comparative *In Vitro* Susceptibility of Gram-negative Bacteria to Levofloxacin

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A multicentre study of the comparative susceptibility of a wide range of clinically important Gram-negative species to levofloxacin was undertaken. 3316 isolates (2052 *Enterobacteriaceae;* 412 *Ps. aeruginosa;* 162 *H. influenzae;* 140 *M. catarrhalis;* 186 *Neisseria spp.;* 364 others) were collected from 20 European centres during 1993–1994. MICs of levofloxacin (LVFX), ofloxacin (OFX), ciprofloxacin (CPFX), sparfloxacin (SPFX) and nalidixic acid (NAL) were determined using the NCCLS agar incorporation method. LVFX was very active against species of the *Enterobacteriaceae* with MIC_{90} for the majority of species in the range 0.03–0.5 mg/l. The relative potency of the four fluoro-quinolones against these isolates was: CPFX > LVFX/SPFX > OFX. However, the overall difference between the compounds was seldom greater than 2-fold. LVFX showed good activity against *Ps. aeruginosa* with 80% of 412 isolates inhibited by ≤2 mg/l. Against this species, LVFX was twice as active as OFX/SPFX and 4-fold less active than CPFX. All of the fluoroquinolones tested demonstrated potent antibacterial activity against other Gram-negative species including: *Haemophilus* spp., *M. catarrhalis, Neisseria* spp., *B. pertussis, L. pneumophila, Vibrio* spp., *C. jejuni, H. pylori, A. hydrophila* and *P. shigelloides* with MIC_{90} in the range 0.015–0.06 mg/l. These results demonstrate the broad-spectrum potent antibacterial activity of LVFX against Gram-negative species which, when considered together with its superior pharmacokinetics to CPFX, the most active of the compounds tested, suggest it will have an important role in the treatment of a wide range of infections caused by these organisms.

P1151 Serum Bactericidal Activity of Levofloxacin

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Objectives: To determine the serum bactericidal activity (SBA) of levofloxacin following a single 500 mg oral dose to twelve healthy volunteers.

Methods: Todd-Hewitt-Broth (microdilution method. NCCLS, M21-T) supplemented with lysed horse blood was inoculated with 13 *S. pneumoniae* strains (10^5 CFU/ml). >99.9% reduction after an over-night incubation was defined as serum bactericidal titre (SBT). SBT was calculated by log transformation of each reciprocal bactericidal titre, where <1:2 was handled as 1:1. All experiments were repeated twice. Quality control strains were *E. coli* ATCC 25922, *S. aureus* ATCC 25923 and *S. aureus* Oxford 6571.

Results:

Table: Duration (h) of SBA greater that SBT dilution 1:2

Strain	Duration	Strain	Duration	Strain	Duration
7724	3.57	33, 229**	3.40	6796	4.32
713	1.33	18, 055	0.75	17, 077	5.98
32, 475**	6.31	15, 135	6.31	16, 000*	3.40
15, 357	5.40	20, 224	3.16	40, 932*	2.74
13, 904	3.32				

* Penicillin resistant, ** Penicillin and Cefotaxime resistant.

Mean 3.85 h, SD 1.77, CV% 46.1, SEM 0.49, Min 0.75, Median 3.40, Max 6.31, Range 5.56

The mean duration of SBA for the QC strains: *E. coli* >24 h, *S. aureus* Oxford 10 h and ATCC 10.6 h.

Conclusions: Serum levels achieved following 500 mg levofloxacin resulted in SBA (SBT >1:2) from 0.75 to 6.3 h, which was independent of sensitivity to penicillin and cefotaxime.

P1152 Intracellular Activity of Ciprofloxacin and Bay 12-8039

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Objectives: The intra- and extracellular activity of Ciprofloxacin (CIP) and Bay 12-8039 (BAY) against *Staphylococcus aureus* (SA) showing various antibiotic susceptibility pattern.

Methods: Polymorphonuclear leukocytes (PMN) and pre-opsonised SA (Oxford NCTC 6571, ATCC 25923 and six MRSA) were incubated at a ratio of 1:1 for 15 minutes at 37°C. Extracellular bacteria were removed by differential centrifugation. Phagozytised bacteria were incubated with 0.1, 1, and 10 fold MIC. Aliquots were taken during 4 hours and the number of viable bacteria (CFU/ml) was determined by subculture technique.

Results: The MIC of CIP was 0.5 μg/ml and $\geq$16 μg/ml respectively. The MIC of BAY was 0.063 μg/ml and 2 μg/ml respectively. The table shows the % of CFU/ml without/with PMN after 4 h of incubation.

	SA Oxford NCTC 6571 SA ATCC 25923	MRSA sensitive to CIP	MRSA resistant to CIP MR-CIP RSA
0.1 MIC Cip	133 (268)	170 (367)	281 (183)
1 MIC Cip	116 (101)	151 (106)	114 (97)
10 MIC Cip	24 (10)	15 (10)	89 (86)
0.1 MIC Bay	94 (190)	224 (339)	323 (278)
1 MIC Bay	124 (169)	171 (178)	210 (168)
10 MIC Bay	66 (40)	39 (5)	43 (2)

Conclusions: Against test strains and MRSA both BAY and CIP were equally active, against MR-CIP-RSA BAY was more cidal against extra-and intracellular *Staphylococci*.

P1153 Activity of BAY 12-8039 against Gram-Positive Cocci

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Objectives: To compare the in vitro activity of BAY 12-8039 with that of other antibiotics used for infection by gram-positive cocci.

Methods: 371 gram-positive cocci, blood isolates, were tested for their susceptibility to BAY 12-8039 (BAY), ciprofloxacin (CIP), sparfloxacin (SPA), trovafloxacin (TRO), lomefloxacin (LOM), levofloxacin (LEV), vancomycin (VAN), teicoplanin (TEI), erythromycin (ERY), clarithromycin (CLA), imipenem (IMI) and meropenem (MER) with microbroth dilution.

	MIC90 (mg/L)											
	BAY	CIP	SPA	TRO	LOM	LEV	VAN	TEI	ERY	CLA	IMI	MER
S. pneu	0.1	1	0.2	0.1	4	1	0.2	0.1	0.1	0.1	0.1	0.1
S. pyo	0.1	0.5	0.2	0.1	4	0.5	0.2	0.1	0.1	0.1	0.1	0.1
MSSA	0.1	1	0.1	0.1	2	0.2	1	0.5	0.2	0.1	0.1	0.1
MRSA	8	32	16	8	32	16	4	1	32	32	16	16
S. haem	4	32	32	8	32	16	2	8	32	32	8	16
MSSE	0.1	4	0.1	0.1	2	4	2	2	0.1	0.1	0.1	0.2
MRSE	2	32	16	8	32	8	2	4	32	32	4	8
E. faec	16	32	16	16	32	32	2	0.1	32	32	0.5	4
E. fium	32	32	32	32	32	32	0.5	0.2	32	32	32	32
S. bovis	0.2	2	0.5	0.5	16	2	0.2	0.1	32	32	0.1	0.1
S. mit	0.2	16	1	0.1	32	4	0.2	0.1	32	32	0.1	0.5

Results: The MICs90 of all antibiotics (MIC90) are shown in the table. BAY 12-8039 was the most effective quinolone against pneumococci, streptococci and methicillin susceptible staphylococci, it was not effective against enterococci (only 50% of *E. faecalis* were susceptible), MRSA and *S. haemolyticus*.

Conclusions: Bay 12-8039 shows a promising in vitro activity and may be a welcome drug in the treatment of pneumococcal and streptococcal infections.

P1154 Activity of BAY 12-8039 against Aerobic and Anaerobic Gram-Positive Rods

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Objectives: To compare the in vitro activity of BAY 12-8039 with that of other antibiotics used for infection by gram-positive rods.

Methods: 129 gram-positive rods from clinical materials were tested for their susceptibility to BAY 12-8039 (BAY), sparfloxacin (SPA), trovafloxacin (TRO), clinafloxacin (CLF), erythromycin (ERY), clarithromycin (CLA), clindamycin (DAL), imipenem (IMI), meropenem (MER), augmentin (AUG), piperacillin (PIP) and metronidazole (MET) with microbroth dilution.

Results: The MICs90 of all antibiotics are shown in the table. BAY 12-8039 and clinafloxacin were the most active quinolones, they were the only antibiotics with any activity against *Corynebacterium JK*.

	MIC90 (mg/L)											
	BAY	SPA	TRO	CLF	ERY	CLA	DAL	IMI	MER	AUG	PIP	MET
Listeria	0.5	2	0.1	0.2	0.2	0.1	4	0.1	0.1	0.5	8	–
CorJK	2	32	16	2	32	32	32	32	32	64	64	–
Actinomy	0.2	0.5	0.2	0.1	0.1	0.1	0.1	0.1	0.1	0.2	0.5	32
Nocardia	8	16	16	2	32	16	32	16	16	64	64	–
Bifidob	2	4	4	1	0.1	0.1	0.2	0.1	0.1	0.2	0.5	32
Clostdif	2	4	1	1	1	1	2	0.5	0.2	0.2	1	0.5

Conclusions: Bay 12-8039 may be an alternative for the treatment of infections by *Listeria, Actinomyces* and *Corynebacterium JK*.

P1155 The Postantibiotic Effect of BAY 12-8039

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The postantibiotic effects (PAE) of BAY 12-8039, a new fluoroquinolone on 3 strains of *Escherichia coli, Staphylococcus aureus, Haemophilus influenzae, Streptococcus pyogenes* and *Streptococcus pneumoniae* were investigated. BAY 12-8039 solutions were added to log phase cultures of approximately 10^5 cfu/mL to give concentrations equivalent to 1, 4 and 10 × MIC. Cultures were shaken at 37°C for 1 h, the BAY 12-8039 concentration was then reduced by 1000-fold dilution and incubated at 37°C for 24 h. Viable counts were performed prior to exposure, hourly for 6 h and at 24 h after dilution. Bacteria were enumerated after 24 h incubation at 37°C. PAE was defined as PAE = T − C, where T is the time required for the count in the test culture to increase 1 $\log_{10}$ above the count observed immediately after dilution and C is the equivalent time for the control. BAY 12-8039 exhibited a significant concentration dependent PAE with both Gram positive and negative organisms, ranging at 1, 4 and 10 × MIC from 0 to 2.2 h, 1.2 to 3.1 h and 1.4 to 3.3 h respectively. BAY 12-8039 exhibited concentration dependent PAE similar to that of other fluoroquinolones.

P1156 *In Vitro* Activity of BAY 12-8039

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The in vitro activity of BAY 12-8039 (1-cyclopropyl-7 [(S,S)-2,8 diazabicyclo [4.3.0] non-8-yl]-6-fluoro-8-methoxy-1, 4-dihydro-4-oxo-3-quinoline carboxylic acid), a new fluoroquinolone, was determined against a wide range of clinical bacterial isolates and compared with that of ofloxacin. BAY 12-8039 was highly active against all Gram positive species tested being generally 4–8 times more active than ofloxacin against fluoroquinolone-susceptible (MIC ofloxacin $\leq$2 mg/L) isolates (MIC_{90} [mg/L] *Staphylococcus* spp. 0.12, *S. pneumoniae* 0.12, *E. faecalis* 0.25 mg/L). BAY 12-8039 was also highly active against isolates of *H. influenzae* (MIC_{90} 0.06), *M. catarrhalis* (MIC_{90} 0.12), *Neisseria* spp. (MIC_{90} 0.03), *Legionella* spp. (MIC_{90} 0.015), ofloxacin-susceptible isolates of the Enterobacteriaceae (MIC_{50} range 0.03–0.5), *Campylobacter* spp (MIC_{90} 0.5) and *Vibrio* spp. (MIC_{90} 0.25). BAY 12-8039 was somewhat less active against isolates of *Ps. aeruginosa* (MIC_{90} 2). BAY 12-8039 was very active against *M. pneumoniae* (MIC_{90} 0.12), *M. hominis* (MIC_{90} 0.06), *U. urealyticum* (MIC_{90} 0.06), *C. trachomatis* (MIC_{90} 0.12), *C. pneumoniae* (MIC_{90} 0.12) and *M. tuberculosis* (MIC_{90} 0.25). BAY 12-8039 was also active against obligate anaerobes including *B. fragilis, Prevotella melaninogenica* and *Fusobacterium* spp. (all MIC_{90} 1) and against *Peptostreptococcus* spp. (MIC_{90} 0.25), *C. perfringens* (MIC_{90} 0.5) and *C. difficile* (MIC_{90} 1). These results demonstrate the broad spectrum antibacterial potency of BAY 12-8039 which includes, in particular, Gram positive bacteria and a wide range of pathogens of the respiratory tract.

P1157 Susceptibility of Anaerobic Bacteria to BAY 12-8039, a New Fluoroquinolone

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Objectives: The aim of the present investigation was to determine the in vitro activity of BAY 12-8039 compared with other antimicrobial agents against anaerobic bacteria.

Methods: The activity of BAY 12-8039 was determined against 360 clinical isolates of anaerobic bacteria by the agar dilution method and were compared with levofloxacin, trovafloxacin, cefoxitin, imipenem, clindamycin and metronidazole.

Results: BAY 12-8039 and imipenem were the most active agents tested. Anaerobic cocci (50 strains) had the following minimum inhibitory concentrations: BAY 12-8039, range 0.125–1.0 mg/l; imipenem, range 0.016–0.064 mg/l. *Propionibacterium acnes* (30 strains): BAY 12-8039, 0.064–0.5 mg/l; imipenem, 0.032–0.064 mg/l. *Clostridium perfringens* (30 strains): BAY 12-8039, 0.25–1.0 mg/l; imipenem, 0.016–0.5 mg/l. *Clostridium difficile* (50 strains): BAY 12-8039, 1.0–2.0 mg/l; imipenem, 4.0–8.0 mg/l. *Bacteroides fragilis* (50 strains): BAY 12-8039, 0.125–1.0 mg/l; imipenem, 0.064–0.25 mg/l. *Bacteroides, Porphyromonas* and *Prevotella* species (100 strains): BAY 12-8039, 0.125–0.25 mg/l; imipenem, 0.016–0.25 mg/l. Fusobacteria (50 strains): BAY 12-8039, 0.25–1.0 mg/l; imipenem, 0.008–0.064 mg/l.

Conclusions: BAY 12-8039 may be useful as treatment and prophylaxis for infections due to anaerobic bacteria.

Macrolides, streptogramins and miscellaneous antibiotics

P1158 In-Vivo Pharmacodynamic Parameters Describing Efficacy of Quinupristin/Dalfopristin Against Multiple Bacterial Pathogens

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The neutropenic mouse thigh-infection model was used to determine the pharmacokinetic/pharmacodynamic (PK/PD) parameter best describing antimicrobial activity of the new streptogramin RP59500 (RP). RP is a combination of two semi-synthetic pristinamycin derivatives, quinupristin (Q) and dalfopristin (D), which displays strong synergistic effect against gram-positive organisms, including those resistant to known antibiotics. Finding the PK/PD parameters predicting efficacy is important because Q, D, and RP MICs exhibit wide variation and do not reflect in-vivo response. Mice were infected with 4 strains of methicillin-susceptible (2 MSSA) and -resistant (2 MRSA) *S. aureus* and 11 strains of penicillin-susceptible (1 PSSP), -intermediate (4 PISP), and -resistant (6 PRSP) *S. pneumoniae*. Both MRSA, 3 PISP and 4 PRSP were erythromycin-resistant. Mice had 7.04 $\pm$ 0.65 $\log_{10}$ CFU/Thigh when treated for 24 h with RP 2.5–1280 mg/Kg divided into 2 or 4 doses. A sigmoid dose-response model was used to estimate, by non-linear regression, the dose required to produce a net bacteriostatic effect over 24 h (static dose) and the correlation of PK/PD parameters with in vivo efficacy of RP. Stepwise regression analysis was used to estimate the PK/PD parameter best predicting static dose of RP. Q MIC, but not D MIC or RP MIC, predicted static dose of RP (R^2 = 91, 0.4, and 20%, respectively). Of all parameters, RP AUC/MIC + Q AUC/MIC exhibited the greatest correlation with efficacy (R^2 = 67%). Q, D, and RP AUC/MIC ratios, alone (R^2 = 43, 30, and 62%, respectively) or in any other combination, do not reflect the efficacy of RP as well as the addition of RP + Q ratios.

P1159 Antipneumococcal Activity of RP59500 (Quinupristin/Dalfopristin) as Determined by MIC and Time-Kill-Curves

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Objectives: Determination of the antipneumococcal activity of the first injectable streptogramin combination RP59500 (quinupristin/dalfopristin) by MIC and time-kill-curves.

Methods: The in vitro activity of RP59500 against a group of 93 pneumococcal isolates from systemic infections was determined by the standard agar dilution method according to the recommendations of the National Committee of Clinical Laboratory Standards.

Results: Of the isolates, 32 were penicillin-sensitive (Pen-S) and erythromycin (Ery-S), 30 erythromycin-resistant (Ery-R) and Pen-S, and 31 were penicillin-intermediate (Pen-I) and Ery-S. Against the first group of strains (Pen-S, Ery-S) RP59500 showed good activity (MIC_{90} = 0.5 mg/L). Similar results were obtained for the Pen-I Ery-S group of the strains (MIC_{90} = 0.5 mg/l). Ery-R strains were slightly less susceptible (MIC_{90} = 1 mg/l). Time kill testing of 3 Ery-S clindamycin-susceptible (Clin-S), 3 Ery-R clindamycin-resistant, and 3 Ery-R Clin-S strains were performed at 0, 1, 2, and 4 h. RP59500 yielded rapid killing.

Conclusions: In view of the good activity against all pneumococci tested, including Pen-I and Ery-R isolates, RP59500 might